I. AMENDMENTS

A. In the Specification

Please amend the first paragraph, at page 1, as follows:

This application is a continuation of U.S. Serial No. 09/225, 904, filed January 5, 1999, which is a Divisional of U.S. Serial No. 08/497,535, filed June 30, 1995 (now U.S. Patent No. 5,856,094), which is a continuation-in-part of **[[U.S. Serial No. _____]]** U.S. Serial No. 08/439,962, filed May 12, 1995 (now U.S. Pat. No. 5,767,258), the entire content of each of which is incorporated herein by reference.

Please amend the second paragraph following "Brief Description of the Drawings" at page 8 as follows:

Figure 1b shows the genomic organization of 5'ALT. Coding exons for $p15^{INK4B}$ and $p16^{INK4A}$ are designated by black boxes. E1=exon 1, E2=exon 2 and E3=exon 3. 5'ALT is located between exon 1 and 2 of $p15^{INK4B}$ and approximately 30 ~~Kb upstreat~~ kilobases (kb) upstream of exon 1 of $p16^{INK4A}$.

Please amend the second full paragraph at page 8 as follows:

Figure 3b shows the nucleotide sequence (SEQ ID NO:1)of the first exon of p16.

Please amend the paragraph bridging pages 29-30 as follows:

The present invention provides a method of treating a cell proliferative disorder associated with expression of 5'ALT or 5'ALT-p16 or -p15 polynucleotide(s), comprising contacting the cell having or suspected of having the disorder with a reagent which modulates 5'ALT or 5'ALT-p16 or -p15. The term "cell-proliferative disorder" denotes malignant as well as non-malignant cell populations which often appear to differ from the surrounding tissue both morphologically and genotypically. Malignant cells (i.e. cancer) develop as a result of a multistep process. Such

disorders may be associated, for example, with abnormal expression of 5'ALT or 5'ALT-p16 or -p15. "Abnormal expression" encompasses increased, decreased or absent levels of expression of 5'ALT or 5'ALT-p16 or -p15, as well as expression of a mutant form of 5'ALT or 5'ALT-p16 or -p15 such that the normal function of 5'ALT or 5'ALT-p16 or -p15 is altered. Abnormal expression also includes inappropriate expression of 5'ALT or 5'ALT-p16 or -p15 during the cell cycle or in an incorrect cell type. The 5'ALT or 5'ALT-p16 or -p15 polynucleotide in the form of an antisense polynucleotide is useful in treating malignancies of the various organ systems, for example, those of epithelioid origin (e.g., lung, breast). Essentially, any disorder which is etiologically linked to altered expression of 5'ALT or 5'ALT-p16 or -p15 could be considered susceptible to treatment with a reagent of the invention which modulates **[[mcl-1]]** such expression. The term "modulate" envisions the suppression of expression of 5'ALT or 5'ALT-p16 or -p15 when it is over-expressed, or augmentation of 5'ALT or 5'ALT-p16 or -p15 expression when it is under-expressed or when the 5'ALT or 5'ALT-p16 or -p15 expressed is a mutant form of the polypeptide. When a cell proliferative disorder is associated with 5'ALT or 5'ALT-p16 or -p15 overexpression, such suppressive reagents as antisense polynucleotide sequence or 5'ALT or 5'ALT-p16 or -p15 binding antibody can be introduced to a cell. In addition, polynucleotides encoding p16 or p15 can be introduced into the cell to regulate cell proliferation. Alternatively, when a cell proliferative disorder is associated with underexpression or no expression, or expression of a mutant 5'ALT or 5'ALT-p16 or -p15 polypeptide, a sense polynucleotide sequence (the DNA coding strand) or 5'ALT or 5'ALT-p16 or -p15 polypeptide can be introduced into the cell.

Please amend the paragraph bridging pages 53-54 as follows:

Southern blots were performed as described (de Bustros, et al., Proc. Natl. Acad. Sci. U.S.A., 85:5693-5697, 1988). Briefly, 5 mg of genomic DNA were digested with of EcoRI (10 U/mg) alone or in combination with the methylation-sensitive enzymes SmaI, EagI or SacII (15 U/mg each) for 16 h as specified by the manufacturers (Gibco-BRL and New England Biolabs), run on

a 1% agarose gel, transferred to a Zeta-Probe GT nylon membrane (Bio-Rad), and probed with 25 ng of the 0.35 kb and 0.5 kb PCR products of exons 1 and 2 of p16 after random primer ~~labelling~~ labeling (Feinberg, A. P. Vogelstein, B. A, ~~Annal.~~ Anal. Biochem. 137:266-267, 1984). The primer sequences for the PE1 probe are as follows: sense 5' GAAGAAAGAGGAGGGGCTG (~~SEQ ID NO:20~~ SEQ ID NO:22), and antisense 5' GCGCTACCTGATTCCAATTC (SEQ ID NO:21), amplified with an annealing temperature of 60°C by adding 3.6% formamide to the PCR buffer. The c-abl probe was provided by J.-P. Issa. The blots were then exposed in a phosphorimager (Molecular Dynamics). All cases with a partial methylation pattern were repeated to exclude incomplete enzymatic activity.

Please delete the Sequence Listing at pages 77 to 81, and substitute pages 1 to 5 of the Substitute Sequence Listing submitted herewith.